

### REMARKS

Claims 1-8, 10-16, 19-27, and 30-33 are pending and under examination. Claims 1, 4, 6, 14, 19, 23, 26, 30 and 33 have been amended. New claims 34-39 have been added. Support for the amendments and new claims can be found throughout the specification and the claims as filed. In particular, support for the amendment to claims 1, 6, 19, 23, 30 and 33 can be found, for example, on page 4, Summary of the Invention, lines 4-5; in the paragraph bridging pages 10-11; on page 11, first complete paragraph; page 35, lines 18-20; page 56, second paragraph; and page 58, last paragraph. Claims 1, 6, 19, 23, 30 and 33 have also been amended, as well as claims 4, 14 and 26, to correct antecedent basis. Support for new claims 34-36 and 37-39, which merely separately claim members of the Markush group of the base claims, can be found in base claims 19 and 23, respectively. Accordingly, these amendments and new claims do not raise an issue of new matter and entry thereof is respectfully requested. The Office Action mailed July 7, 2008, has been reviewed, and all rejections are respectfully traversed for the reasons that follow.

#### Rejections Under 35 U.S.C. § 101

Claims 1-8, 10-16, 19-27 and 30-33 stand rejected under 35 U.S.C. § 101 as allegedly being directed to non-statutory subject matter. Claims 1, 6, 23, 30 and 34 are asserted in the Office Action to be directed to methods for modeling cellular metabolism of an organism that does not include a physical transformation of matter. Applicants appreciate the indication by Examiner Clow that this rejection could be overcome by amending the claims to recite that a result of the method is “displayed” or “outputted” to a user. Without acquiescing to the reasons for the rejection set forth in the Office Action, Applicants have nevertheless amended claims 1, 6, 23, 30 and 34 to recite “providing an output to a user.”

With respect to claim 19, the Office Action indicates that claim 19 is drawn to a “system” for modeling cellular metabolism of an organism comprising a flux balance analysis model, a plurality of logic constraints and commands for producing an altered flux balance analysis model. Applicants note that a rejection of claim 19 under 35 U.S.C. § 101 was previously withdrawn in the Office Action mailed April 19, 2007. The Office Action of April 19, 2007, acknowledged that “the system is limited to comprise a physical element and is therefore statutory” (emphasis added). Nothing further is set forth in the current Office Action with respect to why the claimed system previously acknowledged by the Office to “comprise a physical element” and to be statutory is no longer considered statutory.

Nevertheless, to further prosecution, claim 19 has been amended to move the recitation of “computer readable medium” from the body of the claim to the preamble so that the preamble recites “[A] computer readable medium having stored thereon a system for modeling cellular metabolism of an organism.” It is respectfully submitted that the computer readable medium of claim 19 is directed to statutory subject.

With regard to claims 16 and 32, Applicants respectfully disagree with the characterization of the teachings in the specification and the interpretation of the step of “engineering” as set forth in the Office Action. In particular, the Office Action states that “the instant application is drawn only to *in silico* modeling and computational representations and procedures (see introduction, page 4, pages 45 and 46 for example).” The Office Action further states that “the step of ‘engineering’ is interpreted as one of *in silico* engineering, and is therefore non-statutory.” Applicants respectfully point out that this interpretation of claims 16 and 32 is contrary to the record and to the acknowledgement of the Office as to the meaning of these claims and their status as being directed to statutory subject matter. In the Office Action mailed September 28, 2006, under the discussion of a previous rejection under § 101, which is noted for the record to have previously been withdrawn, the Office Action explicitly acknowledges on page 3 that claims 16 and 32 are directed to statutory subject matter. “It is noted that ‘engineering a change in an organism’ as recited in claims 16 and 32, is interpreted to be a physical step based on previous arguments. As claims 16 and 32 do recite a physical transformation of matter, they are directed to statutory subject matter and are not rejected herein” (emphasis added). The current Office Action has provided no basis for taking a position contrary to the previous position of the Office other than to erroneously assert that “the instant application is drawn only to *in silico* modeling and computational representations and procedures” (emphasis added). While Applicants acknowledge that the specification teaches *in silico* modeling, such a teaching does not mean that the application is drawn only to *in silico* modeling, as asserted in the current Office Action. To the contrary, the specification teaches that the “results obtained from use of this framework can be applied in a number of areas of research or commercial interest related to metabolic engineering” (page 4, Summary of the Invention). Moreover, one skilled in the art would readily understand that “engineering a change in an organism” refers to engineering an organism rather than “*in silico* engineering,” as asserted in the current Office Action. Applicants respectfully submit that the teachings in the specification have been mischaracterized in the current Office Action and that the interpretation of “engineering a change in an organism” as being one of *in silico* engineering is incorrect. Furthermore, Applicants respectfully

submit that no basis has been provided for the current Office Action to contradict the previous position of the Office that claims 16 and 32 recite a physical transformation and are directed to statutory subject matter.

Applicants respectfully maintain that the claimed methods and system on a computer readable medium, as well as methods that further recite “engineering a change in an organism,” are directed to statutory subject matter. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. § 101 be withdrawn.

#### Rejection Under 35 U.S.C. § 112, Second Paragraph

Claims 1-8, 10-16, 19-27 and 30-33 stand rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite.

In the Office Action, claims 1, 6, 19, 23, 30 and 33 are indicated to recite the phrase “identify boundaries for available flux distributions of a metabolic network.” The Office Action asserts that it is unclear as to what the boundaries represent in the claim. With respect to this phrase, Applicants note that this phrase is recited in claims 1, 6, 19 and 30 but not claims 23 and 33. With respect to this phrase, Applicants respectfully submit that the meaning of “identify boundaries for available flux distributions of a metabolic network” would be clear to one skilled in the art. Applicants respectfully submit that the clarity of this phrase is corroborated by the fact that the phrase “identify boundaries for available flux distributions” was introduced by amendment in the response filed June 30, 2006, and refiled July 28, 2006. None of the Office Actions mailed subsequent to the amendment, including Office Actions mailed September 28, 2006, April 19, 2007, and December 27, 2007, raised the issue of this phrase being unclear, substantiating Applicants’ position that this phrase is clear. Nevertheless, to further prosecution, claims 1, 6, 19 and 30 have been amended to recite “identify stoichiometric boundaries for available flux distributions of a metabolic network.” Applicants respectfully submit that this phrase is clear and definite.

With respect to claim 23, the phrase discussed above is not recited in claim 23. Nevertheless, for consistency, claim 23 has been amended to recite “constrain a stoichiometric boundary for an available flux distribution.” With regard to claim 33, Applicants note that the phrase “identify stoichiometric boundaries for available flux distributions of a metabolic network” is already recited in this claim. Therefore, it is respectfully submitted that the claims are clear as to what the boundaries for available flux distributions of a metabolic network represent.

The Office Action additionally asserts that claims 1, 6, 19, 23, 30 and 33 are unclear for the phrase “wherein said logic constraints constrain a boundary for an available flux distribution” in that it is unclear if the “boundary” is the same as the boundaries recited previously in the claims. Applicants have amended claims 1, 6, 19, 30 and 33 to correct antecedent basis by reciting “one of said identified stoichiometric boundaries.” Regarding claim 23, the term “boundary” is only recited once in the claims and therefore does not have ambiguity with respect to antecedent basis. Accordingly, Applicants respectfully submit that the claims reciting “boundaries” are clear and definite.

The Office Action further indicates that claims 1, 6, 19, 23, 30 and 33 recite the phrase “improved predictive capabilities” but that it is unclear what is being predicted. Although Applicants submit that the claims are clear, nevertheless claims 1, 6, 19, 23, 30 and 33 have been amended to recite “improved predictive capabilities of cellular metabolism of the organism over said flux balance analysis model” to further clarify the improved predictive capabilities. Accordingly, Applicants respectfully submit that the claims are clear and definite.

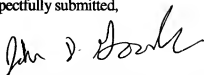
Applicants respectfully submit, for the reasons discussed above, that the claims are clear and definite. Accordingly, Applicants respectfully request that the rejections under 35 U.S.C. § 112, second paragraph, be withdrawn.

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned if there are any questions.

Please charge Deposit Account No. 26-0084 the amount of \$26.00 for one new claim over 20. No other fees or extensions of time are believed to be due in connection with this amendment; however, consider this a request for any extension inadvertently omitted, and charge any additional fees to Deposit Account No. 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,

A handwritten signature in dark ink, appearing to read "John D. Goodhue", is written over the typed name.

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